

Amendments to the Specification

At the indicated page and line numbers, please replace the existing sections or paragraphs, as the case may be, with the ones set forth below.

(Page 10, line 26 through page 11, line 5)

These new restriction sites are situated partly in DNA encoding a linker region near positions where the polyketide synthase is hydrolysed by proteolytic enzymes (vide supra). While some of the restriction sites lie in DNA encoding regions of low homology, others are situated in DNA encoding highly conserved regions (Figure 1 showing SEQ ID NOs: 36, 38, 40, 42, 44, 46, 48, 50, 52, and 54 in the left column from top to bottom and SEQ ID NOs: 37, 39, 41, 43, 45, 47, 49, 51, 53, and 55 in the right column from top to bottom). The introduction of recognition sites for the enzymes AvrII, BglII, Bsu36I and NheI does not change the amino acid sequence in DEBS module 2. In the other five cases (SnaBI, PstI, SpeI, Nsi, HpaI) the amino acid sequence is changed (Figure 2 showing SEQ ID NOs: 36 (left) and 37 (right) and the changes for SnaBI, ~~SEQ ID NO: 56~~; PstI, ~~SEQ ID NO: 57~~; SpeI, ~~SEQ ID NO: 58~~; Nsi, ~~SEQ ID NO: 59~~; and NheI, ~~SEQ ID NO: 60~~). These changes do not affect the activity of the protein (see example 6).

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The two synthetic oligonucleotides Plf and Plb (Figure 4 showing oligonucleotides Plf (SEQ ID NO: ~~61~~ 56) and Plb (SEQ ID NO: ~~62~~ 57) and the oligonucleotides annealed (SEQ ID NOs: ~~63-66~~ 58-61 from top to bottom)) were each dissolved in TE-buffer. 10 μ L of each solution (0.5nmol/ μ L) were mixed and heated for 2 minutes at 65C and then slowly cooled down to room temperature. Plasmid pJLK07 was digested with AvrII and HpaI and ligated with the annealed oligonucleotides. The ligation mixture was used to transform electrocompetent E.

coli DH10B cells and individual colonies were checked for their plasmid content. The desired plasmid pJLK114 was identified by its restriction pattern.

At the indicated page and line numbers, please insert the following paragraph.

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Brief Description of the Figures:

Figure 1 is a schematic drawing showing the location of restriction sites in type I polyketide synthase modules in regions of high homology in erythromycin module 2 (Ery02: SEQ ID NOs 36 and 37) erythromycin module 1 (Ery01: SEQ ID NOs 38 and 39), erythromycin module 4 (Ery04: SEQ ID NOs 40 and 41), erythromycin module 5 (Ery05: SEQ ID NOs 42 and 43), rapamycin module 4 (Rap04: SEQ ID NOs 44 and 45), rapamycin module 7 (Rap07: SEQ ID NOs: 46 and 47), rapamycin module 10 (Rap10: SEQ ID NOs 48 and 49), rapamycin module 13 (Rap13: SEQ ID NOs 50 and 51), avermectin module 1 (Ave01: SEQ ID NOs 52 and 53) and avermectin module 2 (Ave02: SEQ ID NOs 54 and 55).

Figure 2 shows the original amino acid sequence of DEBS module 2 (SEQ ID NOs: 36 and 37) and changes to this amino acid sequence resulting from the introduction of restriction sites for SnaBI, PstI, SpeI, NsiI and NheI.

Figure 3 is a flow chart depicting the construction of plasmids pJLK114 and pJLK117.

Figure 4 provides the oligonucleotide sequences (Plf - SEQ ID NO: 56 and Plb - SEQ ID NO: 57) used to construct the polylinker in pJLK114, and the annealed oligonucleotide construct (SEQ ID NOs 58-61).

Figure 5a is a flow chart depicting the construction of pJLK28, pJLK29 and pJLK41. Figure 5b is a flow chart depicting the construction of pJLK35 and pRIF7.

Figure 6 is a flow chart depicting the construction of pJLK136.

Figures 7a-7f are the nucleotide sequence of the first two modules of the avermectin PKS from *S avermitilis* (SEQ ID NO: 1).